

SEQ ID NO:1:

GGCATATTAGCTTGGGTTACTGTGAATTTTCTGACAGGTCAGCTGCATGGCCACAGA
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 GATGTTTAACAGCACTTATAAGCTCTATACACATAGTTACCTGGGATTTGGATTGAA
 AGCTGCAAGACTAGCAACCCTGGGAGCCCTGGAGACAGAAGGGACTGATGGGCACA
 CTTTCCGGAGTGCCTGT

SEQ ID NO:2:

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 AAATTGCCTCTGCAGGTGTGCGAGCAGGATTGCTTCTGCAACAAAAGCCTCCACCCA
 GCCACATCTTGGGAAAAGAATGGCCACTTCTTGGGGCACAGTCTTTTTCATGCTGGT
 GGTATCCTGTGTTTGCAGCGCTGTCTCCACAGGAACCAGCAGACTTGGTTTGAGGG
 TATCTTCTGTCTTCCATGTGCCCCATCAATGTCAGCGCCAGCACCTTGTATGGAATT
 ATGTTTGATGCAGGGAGCACTGGAACCTCGAATTCATGTTTACACCTTTGTGCAGAAA
 ATGCCAGGACAGCTTCCAATTCTAGAAGGGGAAGTTTTTGAATTCTGTGAAGCCAGGA
 CTTTCTGCTTTTGTAGATCAACCTAAGCAGGGTGCTGAGACCGTTCAAGGGCTCTTA
 GAGGTGGCCAAAGACTCAATCCCCCGAAGTCACTGGAAAAAGACCCCAAGTGGTCCT
 AAAGGCAACAGCAGGACTACGCTTACTGCCAGAACACAAAGCCAAGGCTCTGCTCT
 TTGAGGTAAAGGAGATCTTCAGGAAGTCACCTTTCCTGGTACCAAGGGGCAGTGTTA
 GCATCATGGATGGATCCGACGAAGGCATATTAGCTTGGGTTACTGTGAATTTTCTGA
 CAGGTCAGCTGCATGGCCACAGACAGGAGACTGTGGGGACCTTGGACCTAGGGGGA
 GCCTCCACCCAAATCACGTTCTTCCCCAGTTTGAGAAAACCTCTGGAACAAACTCCT
 AGGGGCTACCTCACTTCCTTTGAGATGTTTAACAGCACTTATAAGCTCTATACACAT
 AGTTACCTGGGATTTGGATTGAAAGCTGCAAGACTAGCAACCCTGGGAGCCCTGGA
 GACAGAAGGGACTGATGGGCACACTTTCGGGAGTGCCTGTTTACCGAGATGGTTGG
 AAGCAGAGTGGATCTTTGGGGGTGTGAAATACCAGTATGGTGGCAACCAAGAAGGG
 GAGGTGGGCTTTGAGCCCTGCTATGCCGAAGTGCTGAGGGTGGTACGAGGAAAAC
 TCACCAGCCAGAGGAGGTCCAGAGAGGTTCTTCTATGCTTTCTCTTACTATTATGA
 CCGAGCTGTTGACACAGACATGATTGATTATGAAAAGGGGGGTATTTTAAAAGTTGA
 AGATTTTGAAAGAAAAGCCAGGGAAGTGTGTGATAACTTGGAAAACCTTCACCTCAG
 GCAGTCCTTTCTGTGCATGGATCTCAGCTACATCACAGCCCTGTTAAAGGATGGCT
 TTGGCTTTGCAGACAGCACAGTCTTACAGCTCACAAAGAAAGTGAACAACATAGAG
 ACGGGCTGGGCCTTGGGGGCCACCTTTACCTGTTGCAGTCTCTGGGCATCTCCCAT
 TGAGGCCACGTACTTCTTGGAGACCTGCATTTGCCAACACCTTTTTTAAGGGGAGGA
 GAGAGCACTTAGTTTCTGAACTAGTCTGGGGACATCCTGGACTTGAGCCTAGAGATT
 WRGTTAATTAASCGGCCGAGCTTATCCTTWATRAGGTAATTTACTTGCMTGGCCGCG
 TTTACACGTCGTGATGGNAACCTGCGTCCCAACTAACGCTTGASAMATCCCCTTCG
 CAGCTGCGATACCAAAAGCCGACGACGCCTTCCACAGTGCCA

Figure 1

SEQ ID NO:3:

MATSWGTVFFMLVVSCVCSAVSHRNQQTWFEGIFLSSMCPINVSASTLYGIMFDAGSTG
TRIHVYTFVQKMPGQLPILEGEVFDSEVKPGLSAFVDQPKQGAETVQGLLEVAKDSIPRSH
WKKTPVVLKATAGLRLPEHKAKALLFEVKEIFRKSPFLVPKGSVSIMDGSDEGILAWV
TVNFLTGQLHGHRQETVGTLDLGGASTQITFLPQFEKTLEQTPRGYLTSEMFNSTYKLY
THSYLGFGGLKAARLATLGALETEGTDGHTFRSACLPRWLEAEWIFGGVKYQYGGNQEG
EVGFEP CYAEVLRVVRGKLHQPEEVQRGSFYAFSYYYDRAVD TDMIDYEKGGILKVED
FERKAREVCDNLENFTSGSPFLCMDLSYITALLKDGFGFADSTVLQLTKKVNNIETGWA
LGATFHLLQSLGISH

Figure 2

CD39Human.seq	M E D T R E S N V E T F S S K N I C A T L G F S S I A A V I A L L A - - - V C L T	36
246 prot	M A T L S W G I V F - - - - - F M V V S C V C S A V S H R N C Q T R F E C I F	31
CD39Human.seq	Q N K - - - - A L P E N T K Y G I V L D A G S S S E T S L Y I V K W P A E E E N D	74
246 prot	L S S M C P I N V S A S T L Y G I M F D A G S T G R I H V Y T F V C K M P C Q	71
CD39Human.seq	T G V V H Q V E E C R V K G P G I S K F V O R V N E I G I Y L T C M E E A R E	114
246 prot	L P L E S E V F D S I V K - P G L S A F V D Q P K Q G A E T V C C L L E V A K D	113
CD39Human.seq	V I P R S Q H Q E T P V Y L G A T A G M R L L R M E S E E L A D R V L D U V E R	154
246 prot	S I P R S H W K K T P V I L K A T A G U R L L - - - P I E H K I A K A L L F E L K E	150
CD39Human.seq	S L S N Y P F D F Q - - - G A R I T G Q E E G A Y G W I T I N Y L L G R F S Q H	192
246 prot	I F R K S I P E L V F K G S V S I M D G S D E G I L A W V T V N F L T Q Q L - - -	187
CD39Human.seq	T E W F S L V P Y E T N N Q E P E G A L D L G G A S T Q V T F V P Q - N Q T I E	231
246 prot	- - - - - H G H R Q E T V I G T L D L G G A S T Q I T F L P Q F E N T I E	216
CD39Human.seq	S P D N A - - - L Q F R L Y G K D Y N V Y T H S E L C Y G K D O A L W C K L A K D	269
246 prot	Q T P R G Y L T S E E M F N S T V K L Y T H S Y L G F G L K A A - - - R L A T L	255
CD39Human.seq	L O V A S N E I L R D P C F H P G Y K K V V N V S D L Y K T P C T K R - F E M T	303
246 prot	G A L E T E G - - - - - T D G H T F R S A C L P R W L E A E	280
CD39Human.seq	L P F O O F - - - - - E I Q G I G N Y O O C H O S I L E L F N T S Y C P Y S O	342
246 prot	W I E G G V K Y Q Y G G N Q E G E V G F E P C Y A E V L R V V R G K - - - - -	314
CD39Human.seq	C A F N G I F L P F L O G E E F G A F S A F - - - Y F V M K F L N L T S E K V S O E	380
246 prot	- - - - - L H Q P E E V Q R G S F Y A F S Y Y Y D R - - - A V D T D M I D Y E	345
CD39Human.seq	K V T E M - M K K F C A Q P W E - - - E I K T S Y A G V K E K Y L S E Y C F S G T	417
246 prot	K G G I L K V E D E E R K A R E V C D N L E N F T S G S P - F L - - - C M D L S	381
CD39Human.seq	V I L S L L L Q G Y H F T A D S W E H I H F I G K I O G S D A G W T L G Y M L N	457
246 prot	V I T A L L K D G F G F A D S T - - - V L Q L T K K V N N I E T G W A L G A T F H	419
CD39Human.seq	L T N M I P A E Q P L S T P L S H S T Y V F L M V L F S L V L F T V A I I G L L	497
246 prot	L L Q S L G I S H	429
CD39Human.seq	I F H K P S Y F W K D M V	510
246 prot		429

Figure 3

1	M A T S W G T V F E M L V V S C V L S A V S E R N Q Q T W F E C I F L S S M C P	246	prot
1	M A T S W G A V F - M L L A A C V G S T V F Y E E Q Q T W F E C V F L S S M C P	mur	ntpase
41	I N V S A S T Y G I M F D A G S T G T R I H V Y T F V Q A M P G Q L F L L E C	246	prot
40	I N V S A C T F Y G I M F D A G S T G T R I H V Y T F V Q K T F C Q L F L L E C	mur	ntpase
81	E V F D S V K P G L S A F V D Q P K Q G A E T V Q C L L E V A K D S I P R S E W	246	prot
80	E I F D S V K P G L S A F V D Q P K Q G A E T V Q I E L L E V A K D S I P R S E W	mur	ntpase
121	K K T P V V L K A T A G L R L L P E H K A K A L L E E V M K E I P R K S P F L V P	246	prot
120	E R T P V V L K A T A G L R L L P E Q K A Q A L L E E V E E I P K N S P F L V P	mur	ntpase
161	K G S V S I M D G S D E G I L A W V T V N F L T G Q L H G H R Q E T V G T L D L	246	prot
50	D G S V S I M D G S Y E G I L A W V T V N F L T G Q L H G R G Q E T V G T L D L	mur	ntpase
201	G G A S T Q I T F L P Q F E K T L E Q T P R G Y L T S F E M F N S T Y K L Y T H	246	prot
200	G G A S T Q I T F L P Q F E K T L E O T P R G Y L T S F E M F N S T F K L Y T H	mur	ntpase
241	S Y L G F G L K A A R L A T L G A L E T E G T D G H T F R S A C L P R W L E A E	246	prot
240	S Y L G F G L K A A R L A T L G A L E A K G T D G H T F R S A C L P R W L E A E	mur	ntpase
281	W I F G G V K Y Q Y G G N Q E G E V G F E P C Y A E V L R V V R G K L H Q P E E	246	prot
280	W I F G G V K Y Q Y G G N Q E G E M G F E P C Y A E V L R V V O G K L H Q P E E	mur	ntpase
321	V Q R G S F Y A F S Y Y Y D R A V D T D M I D Y E K G G I L K V E D F E R K A R	246	prot
320	V R G S A F Y A F S Y Y Y D R A A D T H L I D Y E K G G V L K V E D F E R K A R	mur	ntpase
361	E V C D N L E N F T S G S P F L C M D L S Y I T A L L K D G F G F A D S T V L Q	246	prot
360	E V C D N L G S F S S G S P F L C M D L T Y I T A L L K D G L G F A E R H P L T	mur	ntpase
401	L T K K V M N I E T G W - A L G A T F - - - - - H L L O S L G I S H	246	prot
400	- A H K E S E Q H R D W L G L G G H L S P A P V S G H H Q L R P S S T S E A C I	mur	ntpase
428		246	prot
439	S E P V F S Q E G V D S E T F S D L S G K A W P E T R	mur	ntpase

Figure 4

Apyrase Conserved Regions in CD39-L4

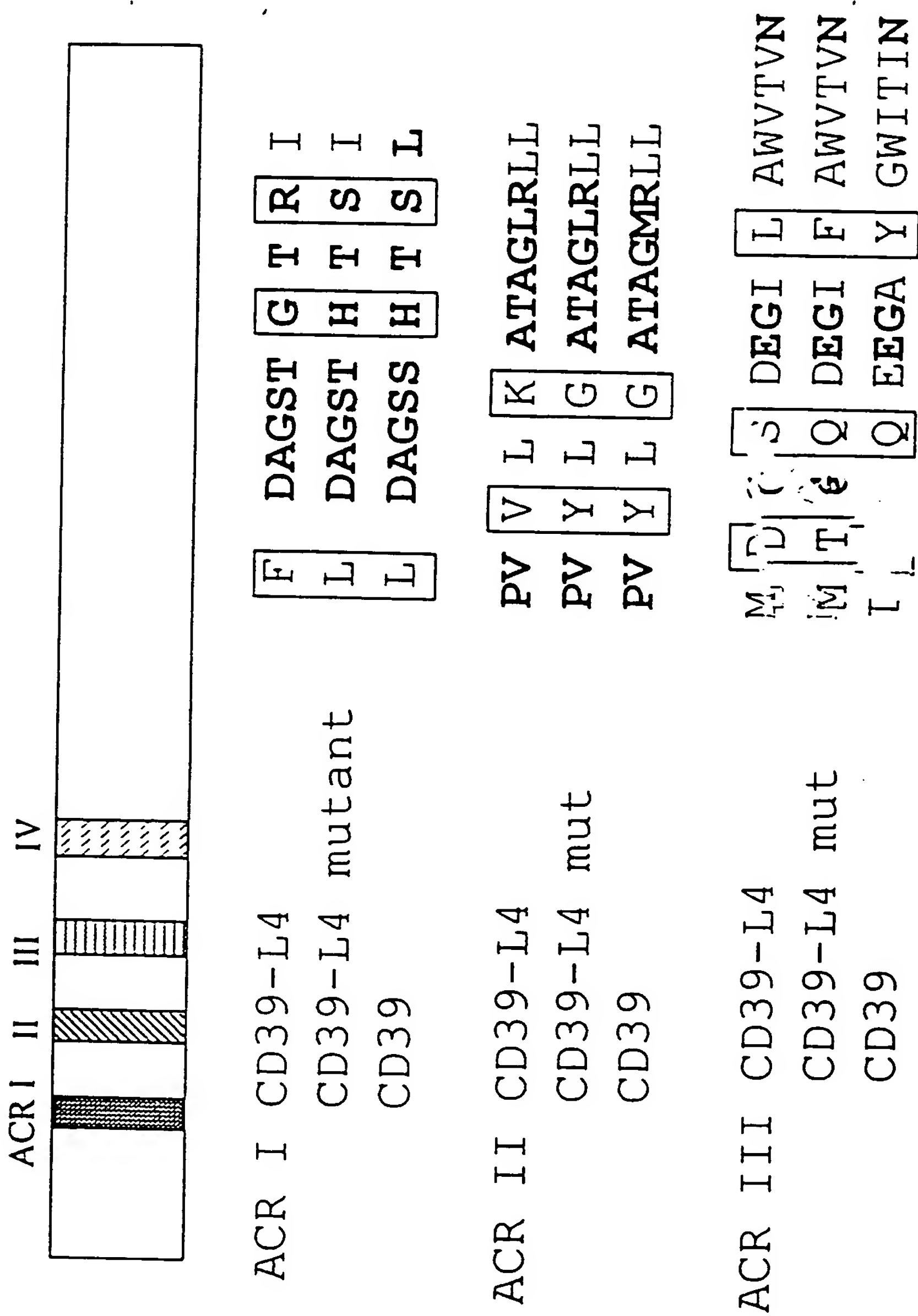


FIG. 5

Nucleotide sequence of the CD39-L4 mutant ACRIII (SEQ ID NO:6). The nucleotide changes have been highlighted. The G to A and A to C changes at positions 502 and 503 produce a Thr, the T to C, C to A and C to A changes at positions 508-510 result in a Gln and the A to C changed at position 525 result in a Phe.

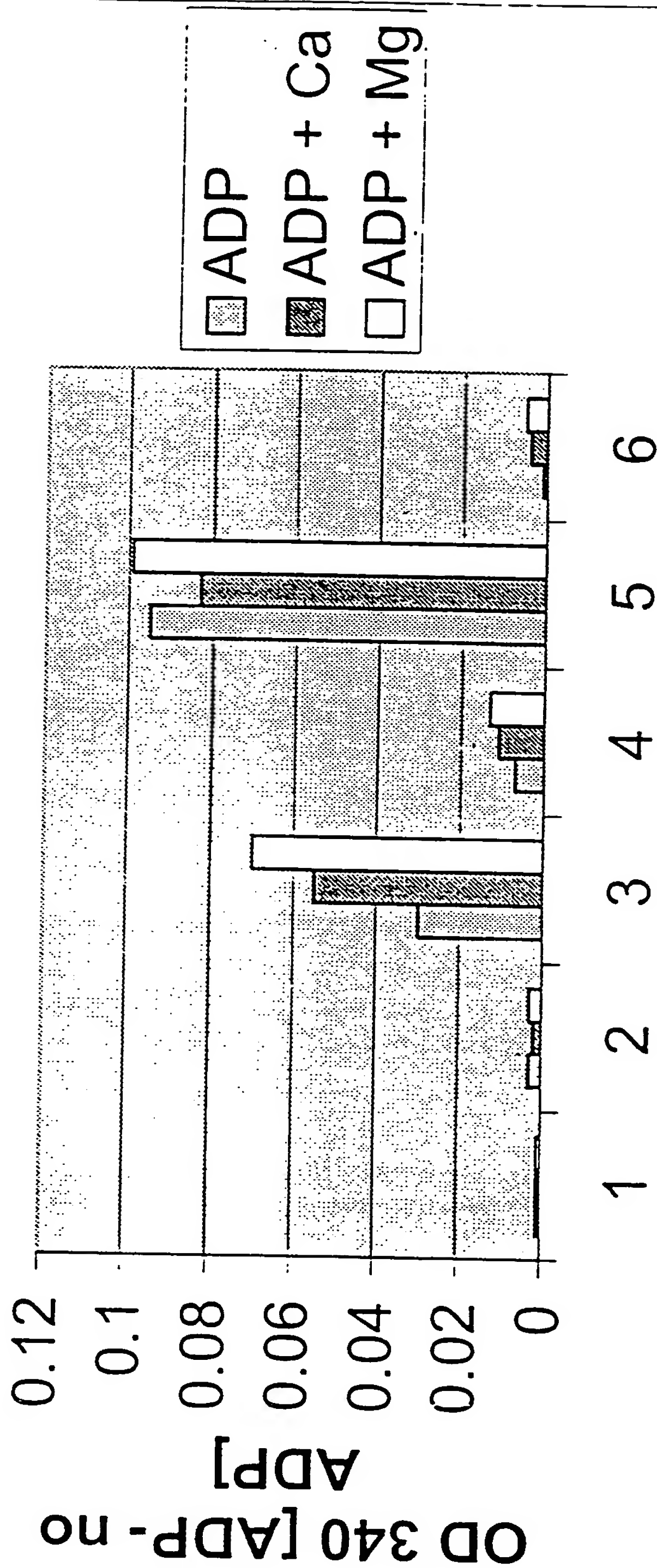
```
ATGGCCACTTCTTGGGGCACAGTCTTTTTTCATGCTGGTGGTATCCTGTGTTTGCAGCGCTGTCT
CCCACAGGAACCAGCAGACTTGGTTTGAGGGTATCTTCTGTCTTCCATGTGCCCCATCAATGT
CAGCGCCAGCACCTTGTATGGAATTATGTTTGATGCAGGGAGCACTGGAACTCGAATTCATGTT
TACACCTTTGTGCAGAAAATGCCAGGACAGCTTCCAATTCTAGAAGGGGAAGTTTTTGATTCTG
TGAAGCCAGGACTTTCTGCTTTTGTAGATCAACCTAAGCAGGGTGCTGAGACCGTTCAAGGGCT
CTTAGAGGTGGCCAAAGACTCAATCCCCCGAAGTCACTGGAAAAAGACCCCAAGTGGTCCTAAAG
GCAACAGCAGGACTACGCTTACTGCCAGAACAAGCCAAGGCTCTGCTCTTTGAGGTAAAGG
AGATCTTCAGGAAGTCACCTTTCCTGGTACCAAAGGGCAGTGTTAGCATCATGACTGGACAAGA
CGAAGGCATATTGGCTTGGGTTACTGTGAATTTTCTGACAGGTCAGCTGCATGGCCACAGACAG
GAGACTGTGGGGACCTTGGACCTAGGGGGGAGCCTCCACCCAAATCACGTTCTGCCCCAGTTTG
AGAAAACCTCTGGAACAAACTCCTAGGGGCTACCTCACTTCCTTTGAGATGTTTAACAGCACTTA
TAAGCTCTATACACATAGTTACCTGGGATTTGGATTGAAAGCTGCAAGACTAGCAACCCTGGGA
GCCCTGGAGACAGAAGGGACTGATGGGCACACTTTCGGGAGTGCTGTTTACCGAGATGGTTGG
AAGCAGAGTGGATCTTTGGGGGTGTGAAATACCAGTATGGTGGCAACCAAGAAGGGGAGGTGGG
CTTTGAGCCCTGCTATGCCGAAGTGCTGAGGGTGGTACGAGGAAAACCTTCACCAGCCAGAGGAG
GTCCAGAGAGGTTCTTCTATGCTTCTTACTATTATGACCGAGCTGTTGACACAGACATGA
TTGATTATGAAAAGGGGGGTATTTTAAAAGTTGAAGATTTTGAAAGAAAAGCCAGGGAAGTGTG
TGATAACTTGGAACAACTTCACC TCAGGCAGTCCTTTCCTGTGCATGGATCTCAGCTACATCAC
AGCCCTGTTA AAGGATGGCTTTGGCTTTGCAGACAGCACAGTCTTACAGCTCACAAAGAAAGT
GAAC AACATAG AGACGGGCTGGGCCTTGGGGGCCACCTTTCACCTGTTGCAGTCTCTGGGCA
TCTCCCATTTGA
```

Amino acid sequence of CD39-L4 mutant ACR III (SEQ ID NO:7). The amino acid changes are D to T (a.a. 168), S to Q (a.a. 170) and L to F (a.a. 175). The changes are shown in bold.

```
MATSYGTVFFMLVVSCVCSAVSHRNQQTWFEGIFLSSMCPINVSASTLYGIMFDAGSTGT
RIHVYTFVQKMPGQLPILEGEVFDVSVKPGLSAFVDQPKQGAETVQGLLEVAKDSIPRSHW
KKTTPVVLKATAGLRLLPEHKAKALLFEVKEIFRKSPFLVPKGSVSIMTGQDEGIFAWVTV
NFLTGQLHGHREQETVGTLDLGGASTQITFLPQFEKTLEQTPRGYLTSEFEMFNSTYKLYTH
SYLGFGGLKAARLATLGALETEGTDGHTFRSACLPRWLEAEWIFGGVKYQYGGNQEGEVGF
EPCYAEVLRVVRGKLHQPEEVQRGSFYAFSYYYDRAVD TDMIDYEKGGILKVEDFERKAR
EVCDNLENFTSGSPFLCMDLSYITALLKDGFGFADSTVLQLTKKVNNIETGWALGATFHL
LQSLGISH
```

FIG. 6

**FIG. 2 ADPase activity of CD39-L4
ACR mutants**



**1) ACR I; 2) ACR II; 3) ACR III; 4)
Wild Type; 5) CD39; 6) Vector**

FIG. 7

SEQ ID No-3	M A T S W G	- - - - -	V F F M L V V S C V C S A V S H R N Q Q T W F E G I F L S S M C P I N V S A S	46
SEQ ID No-5	M A T S W G T	- - - - -	V F F M L V V S C V C S A V S H R N Q Q T W F E G I F L S S M C P I N V S A S	46
CD39Human.seq	M E D T K E S N V K T F C S K N I L A I L G F S I I A V I A - - - - -	L L A V G L T Q - - -	N K A L P E N	46
SEQ ID No-3	T L Y G I M F D A G S T G T R I H V Y T F V Q K M P G Q L P I L E G E V F D S V K	-	P G L S A F V D Q P K Q G	100
SEQ ID No-5	T L Y G I M F D A G S T G T R I H V Y T F V Q K M P G Q L P I L E G E V F D S V K	-	P G L S A F V D Q P K Q G	100
CD39Human.seq	V K Y G I V L D A G S S H T S L Y I Y K W P A E K E N D T G V V H Q V E E C R V K G	P G I S K F V Q K V N E I	101	
SEQ ID No-3	A E T V Q G L L E V A K D S I P R S H W K K T P V V L K A T A G L R L L	- - -	P E H K A K A L L F E V K E I F	152
SEQ ID No-5	A E T V Q G L L E V A K D S I P R S H W K K T P V V L K A T A G L R L L	- - -	P E H K A K A L L F E V K E I F	152
CD39Human.seq	G I Y L T D C M E R A R E V I P R S Q H Q E T P V Y L G A T A G M R L L	R M E S E L A D R V L D V V E R S L	156	
SEQ ID No-3	R K S P F L V P K G S V S I M D G S D E G I L A W V T V N F L T G Q L	- - - - -	H G H R Q E T V	195
SEQ ID No-5	R K S P F L V P K G S V S I M D G S D E G I L A W V T V N F L T G Q L	- - - - -	H G H R Q E T V	195
CD39Human.seq	S N Y P F D F Q - - G A R I I T G Q E E G A Y G W I T I N Y L L G K F S Q K T R W F S I V P Y E T N N Q E T F	209		
SEQ ID No-3	G T L D L G G A S T Q I T F L P Q F E K T L E Q T P R G Y L T S F E M F N S T Y K L Y T H S Y L G F G L K A A	250		
SEQ ID No-5	G T L D L G G A S T Q I T F L P Q F E K T L E Q T P R G Y L T S F E M F N S T Y K L Y T H S Y L G F G L K A A	250		
CD39Human.seq	G A L D L G G A S T Q V T F V P Q - N Q T I E S P D N A - - L Q E R L Y G K D Y N V Y T H S F L C Y G K D Q A	261		
SEQ ID No-3	- - - R L A T L G A L E T E G	- - - - -	T D G H T F R S A C L P R W L E A E W I F G G V K	287
SEQ ID No-5	- - - R L A T L G A L E T E G	- - - - -	T D G H T F R S A C L P R W L E A E W I F G G V K	287
CD39Human.seq	L W Q K L A K D I Q V A S N E I L R D P C F H P G Y K K V V N V S D L Y K T P C T K R - F E M T L P F Q Q F	314		
SEQ ID No-3	Y Q Y G G N Q E G E V G F E P C Y A E V L R V V R G K	- - - - -	L H Q P E E V Q R G S F Y A F S	330
SEQ ID No-5	Y Q Y G G N Q E G E V G F E P C Y A E V L R V V R G K	- - - - -	L H Q P E E V Q R G S F Y A F S	330
CD39Human.seq	- - - - - E I Q G I G N Y Q Q C H Q S I L E L F N T S Y C P Y S Q C A F N G I F L P L Q G D F G A F S A F	363		
SEQ ID No-3	Y Y Y D R - - - A V D T D M I D Y E K G G I L K V E D F E R K A R E V C D N L E N F T S G S P	- F L - - -	C M	378
SEQ ID No-5	Y Y Y D R - - - A V D T D M I D Y E K G G I L K V E D F E R K A R E V C D N L E N F T S G S P	- F L - - -	C M	378
CD39Human.seq	- Y F V M K F L N L T S E K V S Q E K V T E M - M K K F C A Q P W E - - E I K T S Y A G V K E Y L S E Y C F	414		
SEQ ID No-3	D L S Y I T A L L K D G F G F A D S T	- - - - -	V L Q L T K K V N N I E T G W	412
SEQ ID No-5	D L S Y I T A L L K D G F G F A D S T	- - - - -	V L Q L T K K V N N I E T G W	412
CD39Human.seq	S G T Y I L S L L L Q G Y H F T A D S W E H I H F I G K I Q G S D A G W T L G Y M L N L T	- - - - -	- - - - -	402
SEQ ID No-3	A L G A T F H L L Q S L G I S H	- - - - -	- - - - -	459
SEQ ID No-5	- - - - - - - - - - - V L R	- - - - -	- - - - -	423
CD39Human.seq	- - - - - - - - - - - N M I P A E Q P L S T P L S H S T Y V F L M V L F S L V L F T V A I I G L I L I F H K P	495		

FIG 8

FIG. 9

Fig. 9